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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/176,664	10/21/1998	LAWRENCE SALKOFF	018512-00012	2149

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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER
BASI, NIRMAL SINGH

ART UNIT	PAPER NUMBER
1646	24

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/176,664	Applicant(s) Salkoff et al
	Examiner Nirmal S. Basi	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 14, 2002* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 4, 5, 8, 9, 26, 27, and 45-47* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 4, 5, 8, 9, 26, 27, and 45-47* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Amendment filed 11/14/022 has been entered. Applicant has amended claims 1 and canceled claims 48. Claims 1, 4, 5, 8, 9, 26, 27, and 45-47 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action (5/7/02, paper number 22).

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph

3. Claims 1, 4, 5, 8, 9, 26-27 and 45-47 remain rejected, for reasons of record in paper number 23, under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The rejection under 35 35 U.S.C. 101, in paper number 23, is also applied to amended claim 1. Applicant arguments that polynucleotides SEQ ID NOs:2, 17 and 19 encode pH sensitive functional channel proteins is found persuasive. Applicant further argues the present invention is directed to nucleic acids that encode Slo3, a pH sensitive potassium channel expressed in spermatocytes and argues a utility as targets for modulators of spermatocyte function. Applicant arguments have been fully considered but not found persuasive. Applicant and Dr. Timothy Jegla also argued in paper number 22 that intracellular pH has a profound effect on the viability of mammalian sperm, alkaline pH is necessary for sperm capacitation and acrosome reaction, sperm capacitation is accompanied by increase in potassium permeability that hyperpolarizes the membrane, and concluded since Slo3 is highly expressed in sperm and is

activated by alkalization the Slo3 channel plays an important role in sperm capacitation and is an excellent target for candidate compounds that modulate sperm function. Applicants arguments have been fully considered but not found persuasive. The potassium channel of instant invention was isolated from testis. The specification does not disclose that the claimed invention was isolated from spremacocytes as stated by Applicant. Until a showing that the claimed invention was known to be predominantly expressed in the spermacocytes the rejection of record in paper number 23 are maintained. Applicants have submitted Exibits A and B, in paper number 22, two references that Applicants argue alkaline pH is necessary for sperm capacitation and acrosome reaction. Applicants argued since the newly identified Slo3 is highly and specifically expressed in sperm and is activated by alkalinization, persons of skill in the art would expect that the Slo3 channel plays an important role in sperm capacitation, e.g. by increasing potassium permeability, and therefore serve as a target for candidate compounds that modulate sperm function and modulators of Slo3 channel may be used to treat infertility conditions due to Slo3's involvement in capacitation and acrosome reaction. The Exibits provided by Applicant in paper number 22 disclose sperm acrosome reaction is a Ca^{2+} dependent secretory event required for fertilization (Exhibit provided by Applicant, Arnoult et al) and intracellular pH regulates several aspects of mammalian sperm function, although the transport mechanism that control these cells is not understood sperm of many animal species must complete the acrosome reaction, a Ca dependent secretory event, prior to fertilization (Exhibit provided by Applicant, Zeng et al). Although, Slo3 potassium channel is expressed in spermatocytes and it is activated by changes in intracellular pH and membrane potential there is no disclosure in the Exibits

nor specification that show changes in intracellular pH has a profound effect on the viability of mammalian sperm due to Slo3 potassium channel. Alkaline pH is necessary for sperm capacitation and acrosome reaction, but it is due to calcium channel activity (see Exibits A and B provided by Applicant) . Even though the newly identified Slo3 is expressed in testis and is activated by alkalinization there is no disclosure to show it is directly the cause of or even involved in initiating sperm capacitation, e.g. by increasing potassium permeability. Persons of skill in the art may expect that the Slo3 channel may play a role in the spermatocytes but its role is not known at present. Slo3 may serve may serve as a target for candidate compounds but there is no showing said compounds would modulate sperm function and that said compounds may be used to treat infertility conditions due to Slo3's involvement in capacitation and acrosome reaction. Further the examples in the specification do not disclose which channel protein was sensitive to potassium since all the proteins are referred to as Slo3 without reference to SEQ ID NO:.

Applicant also compares instant invention to Example 8 in the "Guidelines for Examination of Application for Compliance with utility requirement". Applicant argues, that in Example 8, a compound A is disclosed to inhibit enzyme XYZ, a well known enzyme, *in vitro*. Applicant compares present application claims to compound A, a nucleic acid that encodes a potassium channel. Applicant argues claimed nucleic acid, like enzymes, have a well established utility in the art. Applicants arguments have been fully considered but not found persuasive. Although, Applicant compares claimed invention to compound A in example 8, no disclosure is provide as to what well known enzyme XYZ it inhibits. The inhibition of a well known enzyme XYZ by claimed invention

could be used to support utility, but none is provided. The utilities asserted by Applicant are not specific or substantial. Since no specific function of the polypeptides of instant invention, or polynucleotides that encode them, are known, and the hypothesized function is based entirely on conjecture from homologous polypeptides, the asserted utilities are not specific to instant polypeptide, but rather are based on family attributes. Neither the specification nor the art of record disclose the claimed nucleic acids, useful to identify drugs that affect said proteins and modulate their activity. Similarly, neither the specification nor the art of record disclose any instances where disorders can be effected by interfering with the activity using claimed polynucleotides. Thus the corresponding asserted utilities are essentially methods of using the claimed polynucleotide to identify other nucleic acids that hybridize to said polynucleotide, or to isolate disease states associated with polypeptide disfunction, and as targets for drug discovery. Therefore the asserted utilities are essentially methods of isolating, testing for or for potentially treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating, isolating or testing for compounds that interact with the claimed polynucleotide, or encoded polypeptide, which may be implicated in an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a “real world” context of use for the claimed polynucleotides, further experimentation is necessary to attribute a utility to the claimed polypeptides and polynucleotide. See Brenner v. Manson, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting

that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Accordingly, the instant specification provides insufficient guidance on "how to use" the claimed polynucleotide of instant invention. Likewise, the instant specification provides insufficient guidance on "how to use" vector containing claimed nucleic acid and cell containing said vector. The rejections of record in paper number 23 are maintained

Claim Rejection, 35 U.S.C. 112, first paragraph

4. Claims 1, 4, 5, 8, 9, 26-27, 45-47 remain rejected under 35 U.S.C. 112, first paragraph, for reasons of record in paper number 23. The rejection under 35 U.S.C. 112, first paragraph, in paper number 23, is also applied to amended claim 1. Applicant argues the present invention describes a family of Slo3 nucleic acids which functionally encode monomers that form potassium channels having a specified unit conductance and potassium channel activity and the methods of detecting and quantification of Slo3 are disclosed in the specification. Applicants arguments have been fully considered but not found persuasive. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, and in paper number 23, one skilled in the art clearly would not know how to use the claimed invention. Since neither the specification nor the art of record disclose any activities or

properties that would constitute a "real world" context of use for the nucleic acids of instant invention, further experimentation is necessary to attribute a utility to the claimed polynucleotides.

Further due to inclusion of hybridization conditions in claim 1, said claim encompasses numerous polynucleotides which, having specific unit conductance characteristics and calcium flux activity, may be completely unrelated, in their mode of cation, to the polynucleotide encoding the polypeptides of SEQ ID NO:1, 16 and 18. Mutated polynucleotides may encode channel polypeptides that have different ligand specificity, since no ligands are disclosed, or be involved in other disease states. Applicant has not disclosed how to use said mutated nucleic acids.

5. No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
January 24, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER